Aquaculture 565 (2023) 739161

Contents lists available at ScienceDirect

Aquaculture

journal homepage: www.elsevier.com/locate/aquaculture

Review

# Bio-utilization of brewery waste (Brewer's spent yeast) in global aquafeed production and its efficiency in replacing fishmeal: From a sustainability viewpoint

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ARTICLE INFO

*Keywords:*
Circularity in aquaculture
Fish meal replacement
Single-cell protein
Fish feed
Sustainable aquaculture

ABSTRACT

Aquaculture contributes significantly to the world's food security. Future aquaculture developments depend mainly on sustainable aquafeed production. Fish meal (FM) is considered unsustainable and not eco-friendly but remains a major protein ingredient in aquafeeds production. The aquaculture sector seeks sustainable protein sources that can reduce the dependency on fishmeal in aquafeeds production. Brewer's spent yeast (BSY) is waste biomass obtained from beer breweries worldwide, and its disposal hazards the natural environment. BSY can be deactivated and used as a single cell protein source in aquafeeds as it has good nutritional value with high protein content (49%) and is cheaper than fishmeal. It also possesses antioxidant and immunostimulant properties. This review focuses on the utility of BSY biomass in aquafeed production. Broken line regression analysis from current literature suggests that the optimal range of BSY inclusion in feed is 10–31.5% for carnivores and 19–31.6% for omnivore fish; FM replacement using BSY is 30–50% for carnivores and 35–80.8% for omnivore fish. Also, the utilization of BSY in the global aquafeed industry could reduce fishmeal usage by up to 13.94% (0.369 MMT) globally and reduce the carbon footprint by about 1.79 megatonnes of CO2e and fish-in-fish-out ratio (FIFO) from 0.82:1 to 0.71:1. Thus, utilization of BSY in the aquaculture sector improves circular bio-economy and environmental sustainability in fish production.

## 1. Introduction

Food insecurity has become a major global challenge since the world's food production needs to feed an estimated 9.7 billion population by 2050 (UN, 2019). A continuous increase in the human development index, especially in developing countries, also brings changes in the human lifestyle and diet consumption patterns. These changes in diet patterns certainly shift towards increased animal protein consumption compared to staple foods in the routine diet (FAO, 2018; 2009). The current global food animal production [337.2 and 156.2 million tonnes (MMT) of meat and fish, respectively (FAO, 2020a, 2020b)], will not be sufficient to meet the future demand. The global animal production for human consumption will need to be increased additional 192 million tonnes (MMT) [133 and 59 MMT of meat and fish production, respectively (FAO, 2020a; Garcia and Rosenberg, 2010)] to mitigate malnutrition in future generations. Fish is one of the preferred animal proteins due to its delicacy and health effects. Fish are rich in protein and an excellent source of essential amino acids and omega-3 fatty acids. Apart from the fact that fishes are low in saturated fat cholesterol, they also contain healthful vitamins and minerals (The Regulation EC N, 1924; UN, 2021). Regular fish consumption improves cardiac health, rejuvenates brain cells, strengthens the immune system, and enhances insulin sensitivity (Ruxton, 2011). Therefore, fish would be a crucial dietary commodity for the betterment of a progressive healthy population in the future (Boland et al., 2013; Golden et al., 2021).

In the present scenario, capture fisheries have reached their maximum sustainable yield in most parts of the world and have minimal scope for further increment in production (FAO, 2020b). On the other hand, aquaculture is a rapidly growing sector, more so than any other animal food-producing sector, which has even outpaced population growth with an average growth rate of 5.3% (FAO, 2020b). Currently,

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https://doi.org/10.1016/j.aquaculture.2022.739161
Received 18 June 2022; Received in revised form 20 October 2022; Accepted 12 December 2022
Available online 14 December 2022

aquaculture is contributing significantly to the world's food security with an annual production of 82.1 MMT, which accounts for over 46% of the world's total fish production and 52% of direct human consumption (FAO, 2020a, 2020b). According to the world bank report, 63% of seafood will be produced through aquaculture by 2030 (Voegele and Anderson, 2014). Further to that, aquaculture is the most efficient converter of feed into protein (30%) than other animal production systems (18% in poultry, 13% in pigs) combined with a reduced carbon footprint (Hasan and Halwart, 2009). Considering these, aquaculture has more scope and responsibility than other food-producing sectors to achieve nutritional security sustainably. Accordingly, it is essential to promote sustainable aquaculture development to ensure future fish production.

Present-day aquaculture developments have resulted from the establishment and standardization of fish breeding & seed production protocols, a better understanding of species-specific nutritional requirements, technological innovations in aquafeed production and enhanced precision through modern management tools in aquaculture practices. All of these conditions have led aquaculture to be an intensified process which has amplified the demand for fish feed. Fish feed accounts for 50–60% of total production costs in modern aquaculture practices (Matulić et al., 2020), and its price mainly depends on its primary ingredients like fish meal, oilseed meals and plant protein concentrates etc. Among those, fish meal (FM) is one of the major protein source ingredients for most high-value carnivorous fishes due to its high-quality protein (600–700 g/kg) with well-balanced amino acids, fatty acid profiles, and essential minerals coupled with their bio assimilation values (NRC, 2011). Current global fishmeal production from capture fisheries (excluding fishmeal from trimmings, 33%) is around 3.84 MMT (24% recovery yield from 16 MMT of forage fish capture), of which 69% is being used for aquaculture feed production (Bachis, 2017; Green, 2018; Pauly et al., 2020). Sustainable aquafeed production demands sustainable ingredients resources, and hence producing fish by feeding with captured wild fish as fishmeal in high inclusion levels is not an economical and ethical way to approach food security. According to Hardy (2010) and Naylor et al. (2021), global forage fisheries for fishmeal production have begun diminishing in the last two decades mainly because of El Nino, and the industry will soon run out of available resources to support the increasing demand for fish feed in the aquaculture sector. Due to the existing demand-supply gap, the price of fishmeal in a global market has already increased (1300–1600 USD/MT) (Indexmundi, 2022; Naylor et al., 2021; World Bank, 2021), indicating that fishmeal will not be economically feasible as well as environmentally sustainable in aquafeed production in the future. Therefore, most research related to fish nutrition and aquafeed production is now mainly focused on evaluating the possibilities and potentialities of non-conventional protein sources, including plant-derived proteins, processed animal by-products, and single-cell proteins (Gupta et al., 2020; Mo et al., 2020; Parolini et al., 2020). Even though recent developments in the production of soy protein concentrates devoid of any anti-nutritional factors have reduced the considerable quantity of fishmeal utilization in aquafeeds, there are many sustainable issues such as intensified crop production and increased needs for land, water and energy and consequent pressure of deforestation (Fry et al., 2016). As in rather, single-cell proteins are sustainable and potential source of nutrients in the future (Glencross et al., 2020), especially yeast (Agboola et al., 2020; Bhattacharjee, 1970), a monocellular eukaryote from the fungi kingdom (Bennett, 1998).

On this regard, Brewer's spent yeast (BSY) is the agro-industrial waste biomass of *Saccharomyces* sp. obtained after fermentation in beer brewing (Ferreira et al., 2010). In beer brewing, the inoculated yeast cells (*Saccharomyces* sp) multiply several times during the fermentation process and produce a surplus quantity of biomass collectively called brewer's spent yeast (BSY) (Huige, 2006). In most developing countries, the viable spent yeast biomass is directly dumped into the open environment, causing deleterious effects on natural fauna and the ecosystem. This viable yeast biomass can be processed into a single cell protein (SCP) mass after deactivating cells by heat or chemical treatment. The dried BSY biomass contains high crude protein content (about 45–50%) with a balanced amino acid profile. Studies on BSY in fish nutrition (primarily as a fishmeal replacer) signify its excellent bioassimilation in fishes compared to other terrestrial animals (Oliva-Teles and Gonçalves, 2001). Other than that, microbially conserved cell wall polymers in BSY, including beta-glucan, chitins and mannoproteins, potentially stimulate innate immune activities, thus increasing disease resistance in cultured fishes. Besides, BSY is cheaper worldwide [0.5–0.6 USD per kg] than most protein ingredients used in aquafeed production. In the last two decades, a decent number of studies have been conducted by reducing the fishmeal inclusion level using BSY biomass in various freshwater and marine fish species diets. However, no review extensively elucidated the bio-utilization potential of BSY in fishes and its efficiency in reducing fishmeal in the diet of different fish species. Hence, this review aimed to comprehensively describe the potentiality and applicability of the BSY biomass in aquafeeds as SCP, emphasizing nutritional quality, fishmeal reduction efficiency, immunostimulatory effects, and its consequent impacts on micro and macroeconomics of the aquaculture sector. We also analyzed the circularity and sustainability aspects of BSY utilization in the aquafeeds in relation to planetary boundaries.

## 2. Brewer's yeast and brewing process

Beer is the most popular alcoholic beverage consumed worldwide, and its health benefits at moderate consumption have been documented (Bamforth, 2007). Beer brewing is an alcoholic fermentation process in which specific yeast species (*Saccharomyces* sp) converts simple sugars into ethanol (Stewart, 2016). Beer can be classified into two groups such as ale and lager (Lodolo et al., 2008), ale beer is produced by top-fermenting yeast (*S. cerevisiae),* and lager beer is the major type and is produced by bottom-fermenting yeast (*S. pastoranus)*. More than a thousand strains of the above-mentioned yeast species are being used in modern brewing industries according to the desired product quality. However, these strains are indifferent in the taxonomical context, even though having immense technical importance in brewing industries (Priest and Stewart, 2006). In this review, the term brewer's spent yeast (BSY) refers to the spent biomass of all yeast strains utilized in beer brewing.

The process of beer brewing (malting, mashing, lautering, brewing, and maturation) and the subsequent filtration of the spent yeast are explained in Appendix A4. Fermentation starts right after the pitching, where cultured pure yeast cells are inoculated adequately without contamination (Wunderlich and Back, 2008). Pitching is a critical step in the beer brewing process, and the pitching rate will depend on the environment conditions, wort quality, and available yeast strain. The standard range of yeast dosage falls around 15–20 million cells/ml at good yeast vitality with proper aeration (Wunderlich and Back, 2008). The inoculated yeast cells multiply 3–6 times during fermentation and produce surplus yeast biomass with pseudoplastic rheology (Huige, 2006). Fermentation is a two-step process, the primary fermentation phase lasts up to the consumption of 90% of all available sugars into alcohol at 8–15 °C, and most of the spent yeast biomass is collected by raking (bottom-fermenting yeast) or skimming (top-fermenting yeast). In modern breweries, the separation of spent yeasts is mainly done by continuous flow centrifugation. The remaining spent yeast is collected after settling down during the second phase of fermentation (lagering phase) done at 1–4 °C (Ferreira et al., 2010). The filtered spent yeast biomass is transferred into various presses and decanting centrifuges with frequent water washing to recover the entrained beer and increase the solid fraction in BSY biomass to around 25–30% (Huige, 2006). The obtained BSY biomass cake is generally reslurried before inactivation.

Inactivation of live spent yeast is done by heat or chemical treatment as early as possible to avoid undesirable quality changes in BSY.

According to Ingledew et al. (1977), heating spent yeast slurry at 60 °C for less than a minute is sufficient to reduce viable yeast cells from more than 108 cells.ml$^{-1}$ to less than one cell.ml$^{-1}$. Heat inactivation can be achieved inexpensively using direct heat exchangers or steam injection. After inactivation, the nutrient-rich yeast slurry is a more desirable medium for the growth of the other microorganisms. Therefore, the inactivated yeast slurry is added with preservatives (organic acids) otherwise dried into powder form (Huige, 2006). In a chemical deactivation, propionic acid or formic acid is used, and they also act as a preservative and ensure the nutrient value of yeast. However, heat deactivation is relatively inexpensive and widely performed (Huige, 2006). Brewer's spent yeast (BSY) is the second major by-product from beer breweries that produced at the rate of 2.35 kg/m$^3$ [2.3 kg/m$^3$ – 3.1 kg/m$^3$ (Huige, 2006); 1.7 kg/m$^3$–2.3 kg/m$^3$ (Hellborg and Piškur, 2008; Pinto et al., 2015)] of the final product. Considering BSY's nutritional quality and environmental impacts, the aquafeed industry can efficiently convert this agro-industrial waste into fish biomass through aquaculture as a part of a bioconversion-based circular economy in a sustainable and eco-friendly way.

## 3. Nutritional quality of BSY

A comprehensive comparison of the chemical composition and amino acid profile of BSY and FM has been presented in Tables 1 & 2. Generally, the nutritional value of the BSY biomass mainly depends on the quality and conditions of the raw material and brewing environment, respectively. The crude protein content of BSY is typically around 49%, with an excellent amino acid profile comparable with fishmeal. The ratio between essential and non-essential amino acids (EAA/NEAA) of BSY biomass is about 0.64, slightly inferior to FM 0.79 (Table 2). The crude AA composition of BSY is well above the standard requirements of most cultured fish species (have been compared in Appendix A5), indicating its suitability as a primary protein source in fish nutrition. Some EAAs like threonine isoleucine are present in higher levels in BSY than FM (Table 2), despite having low arginine, lysine, leucine, and methionine. The nutrient digestibility of BSY varies slightly among different fish species like 76.9% in Nile tilapia (Mmanda et al., 2020), 71.8% in gilthead seabream (Nazzaro et al., 2021), 78.7% in rainbow trout (Nazzaro et al., 2021), 69.7% in salmonids (Heuzé et al., 2018) and 81.5% in Asian seabass (Sorphea et al., 2019) which is averaged about 75.7 ± 4.88%. Even Bertolo et al. (2019), documented 95.3% nutrient digestibility of BSY in In Vitro conditions.

**Table 1**
Comparison of the chemical composition and digestibility estimates of brewer's spent yeast (BSY) with the fish meal (FM) (dry matter basis).

| Nutritional indices | BSY [a] | | | FM [b] | | |
|---|---|---|---|---|---|---|
| | Mean (%) ± SD | Min (%) | Max (%) | Mean (%) ± SD | Min (%) | Max (%) |
| Dry matter (% as fed) | 93.6 ± 1.8 | 89.1 | 97 | 92.2 ± 1.7 | 87.7 | 97.3 |
| Crude protein | 48.9 ± 3.8 | 39.3 | 56.8 | 70.6 ± 3.4 | 58.2 | 78.6 |
| Crude lipid | 4.1 ± 1.2 | 2.2 | 6 | 9.9 ± 1.7 | 6.4 | 13.6 |
| Crude fibre | 1.8 ± 1.3 | 0.1 | 4.4 | Negligible | | |
| NDF^ | 8.8 ± 9.4 | 0 | 20.7 | 5.8 ± 2.6[$] | 3.1 | 9 |
| ADF^ | 2.5 ± 2.5 | 0 | 5.7 | 0.5 ± 0.5[$] | 0 | 1.6 |
| Starch | 10.9 ± 7 | 0 | 17.5 | Negligible | | |
| Total sugars | 1.9 ± 1.3 | 0.3 | 2.8 | Negligible | | |
| Ash | 7.0 ± 1.1 | 5.1 | 9.3 | 18.4 ± 3.1 | 11 0.4 | 28.4 |
| Lignin | 0.8 ± 0.8 | 0 | 1.7 | 0.2 ± 0.2[$] | 0 | 0.3 |
| Gross energy (MJ/kg DM) | 19.6 ± 1.3 | 18.1 | 20.4 | 20.4 ± 1 | 18.4 | 22.8 |
| Energy digestibility # | 69.7 ± NA | 62.6 | 76.8 | 81.7 ± 3.47 | 71.8 | 91.6 |
| Nitrogen digestibility# | 77.1 ± NA | 63.2 | 91 | 87.7 ± 1.18 | 83.1 | 91.7 |

^ NDF – Neutral Detergent Fibre; ADF – Acid Detergent Fibre.
# Digestibility estimates are calculated from salmonids.
[a] (Heuzé et al., 2018); [b] (Heuzé et al., 2015), [$] (Feedtables, 2017a).
Data from Feedipedia (http://www.feedipedia.org) and Feedtables (http://www.feedtables.com).

**Table 2**
Comparison of the amino acid profiles of brewer's spent yeast (BSY) with the fish meal (FM).

| Amino acids (% protein) | BSY | | | FM | | |
|---|---|---|---|---|---|---|
| | Mean ± SEM | Min | Max | Mean ± SEM | Min | Max |
| Essential amino acids (EAA) | | | | | | |
| Arginine | 4.4 ± 0.7 | 3.6 | 5.2 | 6.2 ± 0.9 | 5.0 | 8.9 |
| Histidine | 2.0 ± 0.4 | 1.7 | 2.9 | 2.4 ± 0.5 | 1.6 | 3.3 |
| Isoleucine | 4.6 ± 0.8 | 4.0 | 6.1 | 4.2 ± 0.4 | 3.2 | 4.7 |
| Leucine | 6.2 ± 0.8 | 5.3 | 7.1 | 7.2 ± 0.4 | 6.3 | 8.0 |
| Lysine | 6.3 ± 0.9 | 4.6 | 7.6 | 7.5 ± 0.5 | 6.4 | 8.4 |
| Methionine | 1.5 ± 0.3 | 1.3 | 2.2 | 2.7 ± 0.3 | 2.1 | 3.3 |
| Phenylalanine | 3.6 ± 0.4 | 3.1 | 4.1 | 3.9 ± 0.2 | 3.4 | 4.4 |
| Threonine | 4.4 ± 0.7 | 3.7 | 5.6 | 4.1 ± 0.2 | 3.7 | 4.7 |
| Tryptophan | 1.1 ± 0.2 | 1.0 | 1.4 | 1.0 ± 0.1 | 0.8 | 1.2 |
| Valine | 4.9 ± 0.5 | 4.5 | 5.8 | 4.9 ± 0.4 | 4.1 | 5.5 |
| Non-essential amino acids (NEAA) | | | | | | |
| Alanine | 5.9 ± 1.2 | 4.3 | 6.9 | 6.3 ± 0.3 | 5.7 | 6.9 |
| Aspartic acid | 9.0 ± 2.2 | 7.7 | 12.2 | 9.1 ± 0.6 | 8.0 | 10.9 |
| Cysteine | 0.9 ± 0.6 | 0.5 | 1.9 | 0.8 ± 0.1 | 0.7 | 1.0 |
| Glutamic acid | 14.7 ± 2.2 | 11.4 | 15.8 | 12.6 ± 0.7 | 11.0 | 14.4 |
| Glycine | 4.0 ± 0.3 | 3.7 | 4.3 | 6.4 ± 0.7 | 5.3 | 8.3 |
| Proline | 3.4 ± NA | NA | NA | 4.2 ± 0.4 | 3.6 | 5.3 |
| Serine | 4.3 ± 0.2 | 4.1 | 4.5 | 3.9 ± 0.2 | 3.4 | 4.4 |
| Tyrosine | 2.7 ± 0.1 | 2.5 | 2.8 | 3.1 ± 0.3 | 2.4 | 3.6 |
| **EAA/NEAA** | **0.64** | | | **0.79** | | |

[a](Heuzé et al., 2018); [b](Heuzé et al., 2015). Data from Feedipedia (http://www.feedipedia.org).

The protein digestibility corrected amino acid score (PDCAAS) analysis comparing FM and EAA requirements of model fish species with BSY (Table 3) was carried out to decipher the total digestible/bioavailable EAA prominence of BSY in fish nutrition. In PDCAAS analysis, the crude amino acids levels are digestibility-corrected using average protein digestibility of the corresponding protein ingredients (77.1% for BSY and 87.7% for FM) and subsequently normalized by dividing the available amino acid levels of each ingredient (In this study, FM and standard amino acid requirements of rainbow trout, channel catfish, Nile tilapia, common carp) with the values of the reference ingredient (BSY). The PDCAAS analysis shows that arginine and methionine are two critically limiting EAA in BSY biomass that may not satisfy the requirement of most of the cultured fish species when used as a primary protein source. Therefore, complete replacement of FM by using BSY biomass as a sole protein ingredient is seemingly impossible unless the limiting AAs are augmented in the feed either combinatorially or synthetically. However, a partial replacement can be possible or even beneficial with BSY (will be discussed in the following contexts). The PDCAAS analysis also shows that, except for arginine and methionine, the total digestible EAA levels of BSY suffice the EAA requirements of rainbow trout (0.75 ± 0.07) and channel catfish (0.93 ± 0.13) than to Nile tilapia (1.14 ± 0.14) and common carp (1.09 ± 0.1). The PDCAAS analysis further indicates that histidine and phenylalanine are also limiting in BSY in addition to arginine and methionine in Nile tilapia and common carp, respectively (Table 3). Using the PDCAAS analysis, the nutritional efficacy of BSY can be enhanced in aquaculture by supplementing the limiting AA particularly as per target fish species requirements.

The fatty acid profiles of BSY and FM have been compared in Appendix A1. Fishmeal poses a significantly higher level of free fatty acids (7.3% as DM) than BSY biomass (3.2% as DM). Also, the fatty acid

**Table 3**
Protein Digestibility Corrected Amino Acid Score (PDCAAS) of brewer's spent yeast based on the amino acid requirement and availability in selected fish species.

| EAA* | BSY | Fishmeal | Rainbow Trout | Channel Catfish | Nile Tilapia | Common Carp |
|---|---|---|---|---|---|---|
| **Arginine** | 1 | 1.60 | 1.18 | 1.27 | 1.24 | 1.27 |
| Histidine | 1 | 1.36 | 0.71 | 0.97 | 1.10 | 1.36 |
| Isoleucine | 1 | 1.04 | 0.62 | 0.73 | 0.87 | 0.70 |
| Leucine | 1 | 1.32 | 0.54 | 0.73 | 0.71 | 0.69 |
| Lysine | 1 | 1.35 | 0.86 | 1.05 | 1.05 | 1.17 |
| **Methionine** | 1 | 2.05 | 1.12 | 1.99 | 2.33 | 1.73 |
| Phenylalanine | 1 | 1.23 | 0.72 | 0.76 | 1.37 | 1.19 |
| Threonine | 1 | 1.06 | 0.77 | 0.65 | 1.12 | 1.15 |
| Valine | 1 | 1.14 | 0.69 | 0.79 | 0.74 | 0.95 |
| Tryptophan | 1 | 1.03 | 0.47 | 0.59 | 1.18 | 0.94 |
| **EAA ± SD** | 1 | 1.28 ± 0.31 | 0.75 ± 0.23 | 0.93 ± 0.42 | 1.14 ± 0.46 | 1.09 ± 0.31 |

* EAA - Essential amino acids.

profile of BSY appears to be slightly inferior to the fishmeal. The lipid quality of the feed ingredient is mainly determined by the relative availability of the essential fatty acids (ω6 and ω3) within that (Khoddami et al., 2012). In this regard, the BSY biomass seems to be posing high levels of Non-essential fatty acids (saturated fatty acids) compared to fishmeal. Despite total available omega-6 (ω6) fatty acids in BSY (2.4 $g.kg^{-1}$) is almost similar to the fishmeal (3.2 $g.kg^{-1}$) regardless of total lipid content, more differences were observed in total available omega-3 (ω3) fatty acids between BSY (0.9 $g.kg^{-1}$) and fishmeal (15.8 $g.kg^{-1}$). However, the lipid quality of BSY as a protein ingredient will not potentially affect the final feed lipid quality since fish oil is a primary source of essential fatty acids in fish feeds, and fishmeal poses a major role as a protein source.

Further to the amino acid and fatty acid profiles, BSY biomass also comprises a high level of micronutrients, especially water-soluble vitamins (Vitamin B & C) (Amorim et al., 2019; Ferreira et al., 2010; Jacob et al., 2019; Marson et al., 2020; Vieira et al., 2016). A comprehensive overview of the total available micronutrients in BSY and FM has been presented in Appendix A2. BSY poses almost tenfold levels of most B-vitamins in its biomass than fishmeal. B vitamins are a group of essential compounds crucial in the most physiological process related to energy metabolism DNA synthesis that helps enhance fish growth. The increased levels of fat-soluble vitamins (vitamin D & E) in fishmeal is related to the higher lipid content of fishmeal than BSY biomass. In addition, BSY shows reduced availability of minerals and trace elements in its biomass than fishmeal except for potassium, manganese, copper and molybdenum. This can be attributed to the ash content of fishmeal (18.4% in DM) which is more than twofold higher than in BSY biomass (7% in DM). Despite having low mineral content, BSY (535 $mEq.kg^{-1}$) poses double the value of electrolyte balance (dEB = Na + K – Cl, $mEq.kg^{-1}$) than fishmeal (217 $mEq.kg^{-1}$) and most fish feed ingredients which shown to enhance acid-base equilibrium of feed. Considering these above-mentioned nutritional qualities, the dietary inclusion of BSY would have a beneficial impact on enhancing the nutritional value of the aquafeeds.

## 4. The nucleic acid content in BSY and contradictory viewpoints

Good nutrition not only improves growth but also reflects the health status of cultured animals (Ferreira et al., 2010). As a single-cell protein source, the BSY also poses considerable nucleic acid content (RNA with more purines) in its biomass, in which 12–20% N is associated with nucleic acid (Rumsey et al., 1992). In monogastric animals, the excess dietary nucleic acids, especially purines (Adenine, Guanine and their metabolites Hypoxanthine, Xanthine), get catabolized into uric acid (Clifford and Story, 1976; Sosulski and Imafidon, 1990), which elevates in the blood to a toxic levels (Baker and Molitoris, 1974; Schulz and Oslage, 1976), thus limits BSY usage in livestock and poultry feed production. On the other hand, fishes are ammo-telic animals with altered biochemical and physiological responses to dietary nucleic acids and nitrogen metabolites, eliminating major ammonia load directly via gill instead of converting it into urea (Oliva-Teles et al., 2006). Hence, the tolerable limit for dietary nucleotides is always higher in fishes than in any other ureotelic animals (Kinsella et al., 1985). Uricase is an enzyme (urate: oxygen oxidoreductase EC. 1.7.3.3) produced in the liver that converts uric acid into allantoin and to urea and glyoxylic acid, which is then excreted via urine (Rumsey et al., 1991a, 1991b). The homeostasis capacity of this uricase enzyme differs among the animals, and there are some shreds of evidence that fish, such as salmonids, pose higher uricase activity and well regulated urolytic pathway that can tolerate higher dietary purine load in their body (Andersen et al., 2006; Kinsella et al., 1985; Rumsey et al., 1991a, 1991b).

$$\textbf{Uric acid} + 2H_2O + O_2 \xrightarrow{\text{uricase}} \textbf{Allantoin} + CO_2 + H_2O_2$$

It is well documented that there is no overriding indication of health issues at an increased level of nucleic acid in the fish diet (Li and Gatlin, 2006), but deficiency will lead to the impaired health status of animals (Grimble and Westwood, 2000). Dietary nucleic acid becomes a conditionally essential nutrient when the animal experiences stress, especially in the captive environment (Hossain et al., 2016), and this is because of insufficient de novo synthesis of nucleotide (Barness, 1994; Cosgrove, 1998). External supplementation of a dietary nucleotide is probably needed to fulfill the nutritional requirements of fish under stress conditions. Low-level dietary nucleotide supplementation often proved beneficial in commercial intensive aquaculture practices (Ferosekhan et al., 2014). However, unlike commercial dietary nucleotides, the nucleic acid in BSY is often combined with nucleoproteins, and they are incredibly stable, reducing their availability via digestion and also the presence of fish nucleases, a prime enzyme of nucleotide digestion, is not well studied (Borda et al., 2003). Thus, augmenting nucleotides at a minimal level in the fish diet by incorporating BSY is often not toxic but beneficial in fish, especially in reducing stress in culture conditions. Apart from stress reduction, dietary nucleic acid inclusion in the fish diet at minimal levels also proved to be enhancing feed attraction (Papatryphon and Soares Jr, 2000), growth (Ferosekhan et al., 2014; Guo et al., 2017; Kader et al., 2018), gut health (Cheng et al., 2011; Reda et al., 2018), disease resistance (Hossain et al., 2016; Kader et al., 2018), reproductive performance (Arshadi et al., 2018; Gonzalez-Vecino et al., 2004) and also reduces nitrogenous waste excretion (Ozório et al., 2010). In this manner, BSY has already been inbuilt with a higher amount of nucleotide content, which will improve the health status of the fish. All these beneficial qualities of BSY make them an ideal and suitable ingredient in aquaculture feed production and an excellent reducer of fishmeal requirements in aquafeeds.

## 5. BSY in FM replacement studies

A decent number of studies have investigated the potential of brewer's spent yeast (BSY) in replacing fishmeal from the diets of various fish species (Table 4). The initial attempt of BSY.

**Table 4**
Summary of studies on the potential of BSY to replace fish meal in the diet of farmed fish and crustaceans.

| Species | IBW (g) | Diet CP (%) | Diet DE (MJ/kg) | Experiment days | BSY inclusion / FM substitution levels (%) | Best BSY inclusion / FM substitution level (%) | Quantity of incorporation (FM: BSY) g/kg of feed | | Weight gain | | Feed conversion | | Protein efficiency | | Reference |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Control | Best | Control | Best treatment | Control | Best treatment | Control | Best treatment | |
| **(Carnivores)** | | | | | | | | | | | | | | | |
| Rainbow trout (*Oncorhynchus mykiss)* | 77.9 | 44 | – | 60 | 10,20% | 20% | 150:0 | 150:200 | 120% | 184% | 1.29 | 1.71 | 1.19 | 1.84 | (Estévez et al., 2022) |
| Rainbow trout (*Oncorhynchus mykiss)* | 206.05 | 41 | 19.9 | 30 | 30% | 30% | 600:0 | 400:300 | 71% | 59% | 1.13 | 1.37 | 2.16 | 1.78 | (Nazzaro et al., 2021) |
| Rainbow trout (*Oncorhynchus mykiss*) | 2.6 | 41 | 13.7 (ME) | 70 | 0,25,50,75% | 25% | – | – | 300% | 333% | 1.17 | 1.11 | 2.08 | 2.2 | (Rumsey et al., 1991a, 1991b) |
| European sea bass (*Dicentrarchus labrax*) | 12 | 48 | 22 | 84 | 0,10,20,30,50% | 30% | 596:0 | 417:329 | 239% | 283% | 1.48 | 1.28 | 1.38 | 1.61 | (Oliva-Teles and Gonçalves, 2001) |
| Gilthead sea bream (*Sparus aurata*) | 113.43 | 44 | – | 60 | 10,20,30% | 30% | 150:0 | 100:300 | 53% | 59% | 2.38 | 2.04 | 0.99 | 1.21 | (Estévez et al., 2021) |
| Gilthead sea bream (*Sparus aurata*) | 253.01 | 41 | 19.9 | 30 | 30% | 30% | 600:0 | 400:300 | 28% | 30% | 1.88 | 1.92 | 1.3 | 1.27 | (Nazzaro et al., 2021) |
| Thai Panga (*Pangasianodon hypophthalmus* X *Pangasius bocourti*) | 36.4 | 32 | 15.3 | 270 | 0,30,45,60,75% | 45% | 300:0 | 165:135 | 1153% | 1548% | 2.6 | 2.4 | 1.2 | 1.3 | (Pongpet et al., 2016) |
| Asian sea bass (*Lates calcarifer*), Tank reared | 22.8 | 44.5 | 15.8 (ME) | 60 | 0,20,37,47% | 47% | 582:0 | 265:468 | 335% | 307% | 1.2 | 1.4 | 1.89 | 1.62 | (Sorphea et al., 2019) |
| Asian sea bass (*Lates calcarifer*), Hapa reared | 44.8 | 44.5 | 15.8 (ME) | 60 | 0,20,37,47% | 47% | 582:0 | 265:468 | 179% | 133% | 1.5 | 1.8 | 1.51 | 1.26 | (Sorphea et al., 2019) |
| Red drum juveniles (*Sciaenops ocellatus)* | 8.01 | 40 | – | 56 | 0,20,30,40,50% | 50% | 285:0 | 143:343 | 630% | 541% | 1.11 | 1.19 | 2.19 | 1.95 | (Rosales et al., 2017) |
| **(Omnivores)** | | | | | | | | | | | | | | | |
| Tilapia (*Oreochromis niloticus*) Clear water | 29 | 35 | 19 | 90 | 0,30,60,100% | 60% | 200:0 | 80:180 | 529% | 535% | 1.58 | 1.45 | 1.81 | 1.97 | (Nhi et al., 2018) |
| Tilapia (*Oreochromis niloticus*) Biofloc | 29 | 35 | 19 | 90 | 0,30,60,100% | 60% | 200:0 | 80:180 | 650% | 604% | 1.28 | 1.35 | 2.26 | 2.12 | (Nhi et al., 2018) |
| Pacu (*Piaractus mesopotamicus*) | 26.6 | 27 | 19 | 54 | 0,30,35,50,70,100% | 50% | 250:0 | 130:190 | 149% | 234% | 1.04 | 1.05 | 3.56 | 3.53 | (Ozório et al., 2010) |
| Climbing perch (*Anabas testudineus*) | 3.29 | 35 | 19.2 | 60 | 0,25,50,75,100% | 75% | 200:0 | 50:200 | 153% | 179% | 2.03 | 1.69 | 1.55 | 1.71 | (Gokulakrishnan et al., 2022) |
| Goldfish (*Carassius auratus*) | 0.56 | 37 | 14 | 84 | 0, 15, 25, 35, 45% | 45% | 400:0 | 220:266 | 550% | 839% | 3.32 | 2.34 | 0.68 | 1.01 | (Gumus et al., 2016) |
| **(Crustaceans)** | | | | | | | | | | | | | | | |
| Giant freshwater prawn (*Macrobrachium rosenbergii*) Clear water | 6.7 | 35 | 19 | 90 | 0,20,40,60% | 40% | 260:0 | 157:155 | 234% | 213% | 5.07 | 5.53 | 0.43 | 0.34 | (Nguyen et al., 2019) |
| Giant freshwater prawn (*Macrobrachium rosenbergii*) Biofloc | 6.7 | 35 | 19 | 90 | 0,20,40,60% | 60% | 260:0 | 105:232 | 233% | 234% | 4.49 | 4.46 | 0.39 | 0.43 | (Nguyen et al., 2019) |

incorporation in the aqua diets as a protein source was in the early nineties by Rumsey et al. (1991a, 1991b), where 25% (250 g.kg$^{-1}$ of feed) dietary inclusion of BSY did not show any adverse effects on growth performances of rainbow trout (*Oncorhynchus mykiss*) fingerlings, and the authors also found a two-fold increase in liver uricase activity of fish fed with the higher BSY concentration diet. However, the potential of BSY as a fishmeal replacer in aqua diets was first realized in European seabass (*Dicentrarchus labrax*) by Oliva-Teles and Gonçalves (2001), where growth and nutrient utilization were not compensated up to 50% replacement of fishmeal (298 g(FM).kg$^{-1}$ of feed) using BSY; on the contrary, the growth performance and nutrient utilization were enhanced at 30% fishmeal replacement (179 g(FM).kg$^{-1}$ of feed) using BSY. To date, multiple studies have elucidated the optimal dietary replacement levels of fishmeal using BSY in various species (Fig. 1), such as 200 g(FM).kg$^{-1}$ of feed in gilthead seabream (*Sparus aurata*) (Nazzaro et al., 2021), 317 g(FM).kg$^{-1}$ of feed in Asian seabass (*Lates calcarifer*) (Sen, 2019), 120 g(FM).kg$^{-1}$ of feed in Nile tilapia (*Oreochromis niloticus*) (Nhi et al., 2018), 142 g(FM).kg$^{-1}$ of feed in red drum (*Sciaenops ocellatus)* (Rosales et al., 2017), 135 g(FM).kg$^{-1}$ of feed in Thai panga (*Pangasianodon hypophthalmus* X *Pangasius bocourti*) (Pongpet et al., 2016), 180 g(FM).kg$^{-1}$ of feed in goldfish (*Carassius auratus*) (Gumus et al., 2016), 120 g(FM).kg$^{-1}$ of feed in pacu (*Piaractus mesopotamicus*) (Ozório et al., 2010), 150 g(FM).kg$^{-1}$ of feed in climbing perch (*Anabas testudineus*) (Gokulakrishnan et al., 2022). And also, in crustaceans, 103 g(FM).kg$^{-1}$ and 155 g(FM).kg$^{-1}$ of feed for clear water and biofloc, respectively, in giant freshwater prawn (*Macrobrachium rosenbergii*) (Nguyen et al., 2019). Even recent studies, also suggest that dietary inclusion of BSY for up to 20 and 30% with only 15 and 10% of FM concentrations in the diet did not affect the growth performances of rainbow trout and gilthead seabream respectively (Estévez et al., 2022; Estévez et al., 2021).

The optimal levels of BSY inclusion and FM replacement in fish diets are seemingly species-specific and depend upon various factors such as individual amino acids requirements, digestive capacity to complex yeast cell-wall compounds to reach inner protein and bioactive molecules, and the ability to cope with nucleotides augmented diet. However, these optimal levels (BSY inclusion and FM replacement using BSY in feed) follow a correlation pattern with the feeding habit of respective fish species. To capture this pattern, an attempt of broken line regression analysis was performed for the full dataset and its subgroups namely omnivores and carnivore fishes to draw better statistical inferences from the available dataset (Fig. 2). The graphs were plotted with BSY inclusion and FM replacement levels in the experimental fish diets against their corresponding normalized weight gain values (NWG %; i.e., control of each experiment considered 100%). Normalized weight gain (NWG%) values were computed from the reported weight gain values in different studies. In total, out of all observations ($n$ = 58) of NWG%, about 65% of observations were higher and 35% of observations were lower than the control diet. Since the majority (65%) of the BSY-fed fish groups ended up with increased weight gain than their respective control diet, it is apparent that the BSY inclusion in the fish diet has decent consistency in enhancing growth in addition to the FM replacement. Furthermore, the segmented trend lines were regressed on the individual graphs for the quantitative estimation of the threshold and breakeven levels of BSY inclusion in the fish diet. Statistically, the full data set elucidates that the BSY inclusion of up to 14.8% in the diet is found to enhance the weight gain (up to 19.2%) of fish and beyond this threshold level, the weight gain is reduced gradually and breakeven the control at 34.6% (Fig. 2A). In an omnivorous fish subgroup, the BSY inclusion of 19% indicates the threshold breakpoint with up to 27.8% growth enhancement and beyond which, the weight gain is affected negatively and breakeven the control at 31.6% (Fig. 2C). Conversely in a carnivorous fish subgroup, the threshold breakpoint is traced at 10% with up to 13.2% growth enhancement and the breakeven point is at 31.5% of BSY inclusion in the diet (Fig. 2E). Parallel to the BSY inclusion, the regression analysis for FM replacement using BSY was also performed for the full dataset that elucidated the threshold and breakeven levels as 26.1% and 75.1% respectively (Fig. 2B). In the omnivore fish subgroup, the 35% FM replacement using BSY serves as a threshold breakpoint and 80.8% as the breakeven point (Fig. 2D). In the carnivore fish subgroup, no significant slope or breakpoint was observed (Fig. 2F). However, the literature data suggest that around 30–50% FM replacement is possible using BSY in a carnivorous fish diet (Table 4). Also taking the ingredient cost and sustainability factor into consideration in addition to the growth performance, the optimal levels of BSY inclusion and FM replacement could be considered between the threshold and breakeven points of the respective subgroups.

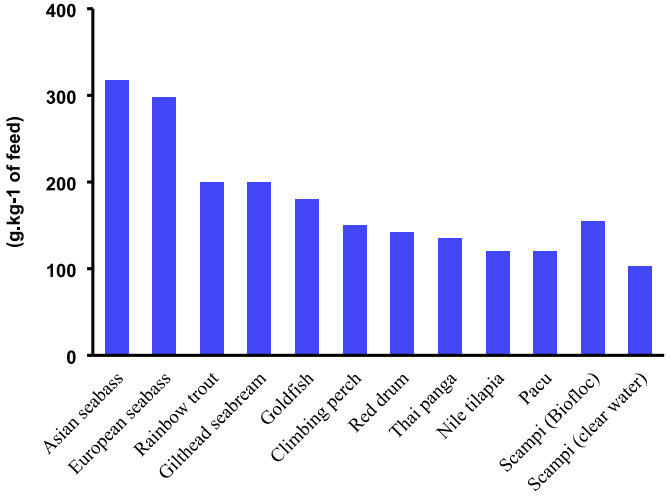



**Fig. 1.** Optimal fishmeal replacement levels (g.kg$^{-1}$ of feed) in the diets of different fish species using BSY.

The illustrations in Fig. 2 show that the optimal range of BSY inclusion and FM replacement in omnivorous fish (19–31.6% BSY inclusion; 35–80.8% FM replacement using BSY) is higher than in the carnivorous subgroup (10–31.5% BSY inclusion; 30–50% FM replacement using BSY) indicating that the bio-utilization efficiency of BSY is comparatively higher in omnivore fish than in carnivores. The twofold increment in the calculated growth enhancement values (27.8% in omnivores and 13.2% in carnivores) at their respective threshold points (Fig. 2C and E) further confirms the BSY efficiency in omnivorous fish diet. The natural diets of omnivore fish consist of relatively higher levels of complex fibers, and their digestive system specifically evolved to digest and mobilize these complex cell wall compounds (chitin, glucan) with the help of gut microbiota (Castro et al., 2013). On the other hand, the digestive system and the gut microbiome of the carnivorous fish species are not habituated to high-fibre diets, thus reducing the bio-utilization capacity of BSY.

Unlike most alternative protein sources, BSY not only involves growth compensation but is rather consistent in enhancing growth and nutrient utilization in fish when partially replaced with fishmeal. This is probably because of the availability of a vast amount of bioactive compounds in BSY biomass that involves in critical physiological processes of the fish. For example, the higher B - vitamins (more than ten folds higher than the FM) in the BSY biomass ensure efficient energy metabolism and DNA synthesis in fish, thus favoring growth. In addition, unlike free purines, the nucleic acid associated purines of BSY have shown to be sparing protein and enhance growth and nutrient utilization in fish (Øverland et al., 2013; Rumsey et al., 1992). Furthermore, the higher dietary electrolyte balance (dEB) of BSY considerably increases the acid buffering capacity of feed that braces acid-base equilibrium of fish to the changing water quality conditions (temperature, pH) in the culture system. Also, the evidence of BSY favoring the gut microbiome and stimulating the production of various extracellular enzymes, which helps the breakdown of complex indigestible fibers, releases entrained

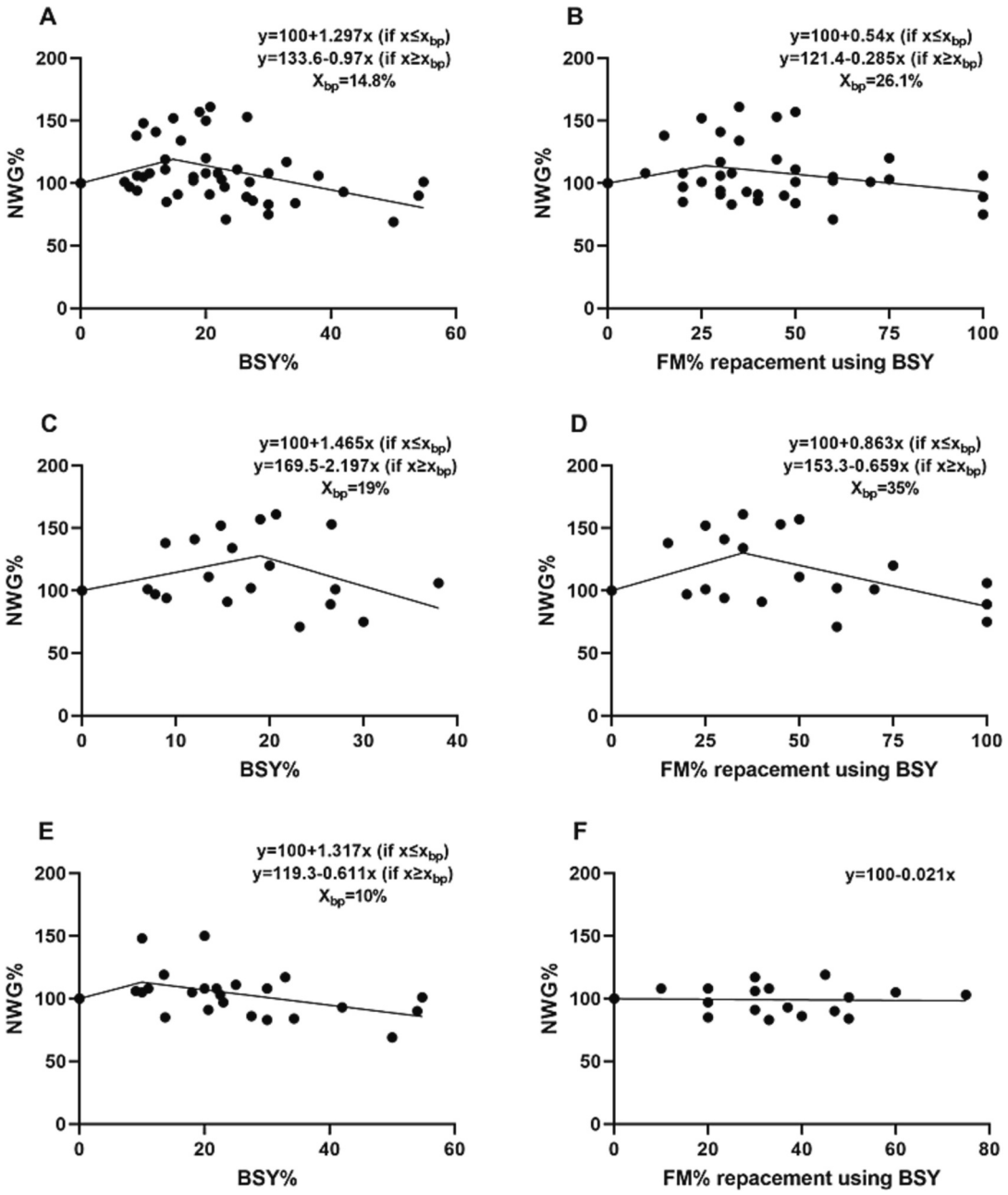



**Fig. 2.** Broken line analysis of normalized weight gain (NWG%; control = 100%) against BSY inclusion and its corresponding FM replacement levels in the diet for Full data set (A, B), omnivorous fish (C, D) and carnivorous fish subgroups (E, F).

proteins and bioactive molecules, thus increasing the nutritional value of the ingested feed. Apart from these, stress reduction and disease resistance during BSY based nutrition may also help in the growth enhancement of the cultured fish (will be discussed in the following context).

## 6. BSY in fish health

Disease outbreaks have become a massive threat in aquaculture production due to intensification. Administration of antibiotics will often have deleterious effects like antibiotic residue and antibiotic resistance (Bondad-Reantaso et al., 2005; Scholz et al., 1999). Hence, there is an enormous need for health-benefiting nutrients in aquaculture to improve fish health conditions without causing adverse effects. BSY is a biomass of yeast, a single cell organism having peculiar polymers in the cell wall called beta-glucans, mannoproteins and chitins (Klis et al., 2006; Lipke and Ovalle, 1998) and health-promoting peptides (Mirzaei et al., 2021; Ribeiro-Oliveira et al., 2021). All these cell wall compounds are proved to have an immunostimulant effect in fish by improving the innate immune system (Bohn and BeMiller, 1995; Herre et al., 2004; Li et al., 2009). Within that, beta-glucan is a major component of the yeast cell wall. It accounts for 50–60%, followed by mannoproteins 35–40% and chitin 1–3% (Bai et al., 2019; Klis et al., 2006; Lipke and Ovalle, 1998). The beta orientation of the yeast cell wall polymer (β glucan) is conserved only in single-cell organisms and can be differentiated from the common alpha-oriented carbohydrate polymers (α glucan) by the first line (non-specific) defense system of animals (Bohn and BeMiller, 1995; Meena et al., 2013). These BSY associated β-glucans directly bind with phagocytes and natural killer cells to produce cytokines molecules that activate lymphocytes (Gantner et al., 2003; Raa, 2000). It also binds with carbohydrate-binding proteins in the hemolymph of shrimp that activates the pro-phenol (proPO) oxidase system in crustaceans (Vargas-

Albores and Yepiz-Plascencia, 2000). Binding usually occurs on specific pattern recognition receptors (PRRs) like dectin1 receptors (Dennehy and Brown, 2007), toll-like receptors (Uematsu and Akira, 2006), lactosylceramide (Zimmerman et al., 1998), complement receptors (Thornton et al., 1996), scavenger receptor (Dennehy and Brown, 2007). These receptor-activated cells produce chemical substances that significantly improve the macrophagic, lysozyme and respiratory burst activity, eventually increasing leucocyte count and relative percent survival (RPS) in fishes (Meena et al., 2013). The recent study on transcriptomic response of gilthead seabream fed with BSY incorporated diet (30%) showed the upregulation of 141 genes in head kidney, liver and anterior-mid intestine out of which, the majority are involved in immunomodulation such as initiation and regulation of inflammation and activation and recruitment of T lymphocytes in fishes (Konstantinidis et al., 2022). Moreover, studies have also documented the immunostimulant effect of BSY as a feed supplement in different fish species (Table 5). These immunostimulant properties of BSY further increase its value in fish nutrition.

Besides immunostimulation, growth-promoting and antioxidant activity have also been documented in fishes fed with BSY. It has been reported that the minimal level (2–5%) of inclusion of BSY as a feed additive in aquafeeds resulted in increased growth responses of fishes (Chotikachinda et al., 2008; Li and Gatlin III, 2003; Matulić et al., 2020; Ran et al., 2016; Zhou et al., 2018). This may be because of the vast bioactive compounds in BSY biomass. One of them is cyclohis-pro (CHP), a non-polar neuroactive peptide that poses solid antioxidant properties coupled with high levels of bio-available vitamin C and free amino acids like glutamic acid, glutamine, and uric acid precursor (purines), collectively involving free radical scavenging in fish (Amorim et al., 2016; Jung et al., 2011; Mirzaei et al., 2015). These bioactive compounds of the BSY reduce the stress load of fish in captive conditions and help rewire the energy towards growth and tissue synthesis instead of re-establishment of homeostasis, thus indirectly promoting the growth of cultured fishes. All these beneficial effects suggest that BSY could be a potential alternative protein source for FM in future fish feed production.

## 7. Environment and economic impact assessment (Macro and micro level)

Even though most scientific research findings for improving aquaculture production express their results in various parameters, economic output and environmental sustainability are the ultimate decider parameter for the long-term adoption at the field level to enhance farmers' income. In that way, an economic and carbon footprint assessment has been made to decipher the need and scope of BSY in aquaculture (Table 6). According to a report by Beroeinc (2017), 46.26 MMT of brewery by-products were produced globally; within that, 12.7% is BSY (in liquid form) accounts for 5.875 MMT. BSY, in its liquid form, usually consists of 10–14% of solid biomass (Huige, 2006). Computing BSY's solid fraction (average 12%), a total of 0.71 MMT of dry BSY (>90% dry matter) is produced worldwide, and the production is still increasing with an annual growth rate of 0.8% every year (Beroeinc, 2017). Even though the market price of dried BSY has been reported as 0.28 USD/kg by (Pongpet et al., 2016), in the present scenario, good quality dried BSY (~49% CP) costs around 0.5–0.6 USD/kg [0.54 USD/kg (Gokulakrishnan et al., 2022); 0.3–0.65 USD/kg (alibaba.com, 2022)] depending on local conditions and final product quality. On the other hand, the price of quality fishmeal (~65% CP) in the past five years ranged between 1.3 and 1.6 USD/kg (Indexmundi, 2022; World Bank, 2021). In the present scenario, a unit cost saving of aquafeed production while replacing every single kilogram of fishmeal by BSY is about 0.72 USD/Kg.

For sustainability assessment, the carbon footprint of global fishmeal production was computed using the value (2.0252 megatonnes $CO_2e$ from 6.963 MMT of forage fish landings) reported by Cashion et al. (2017), and converting it to global forage fish landings for fishmeal production (16 MMT) (Naylor et al., 2021) by assuming the carbon

**Table 5**
Immunostimulant effect of BSY in fishes.

| Species | Experiment duration | BSY Dosages (%) | Optimal dosage (%) | Immune performance enhancement | | References |
|---|---|---|---|---|---|---|
| | | | | Control | Best treatment | |
| Hybrid striped bass (*Morone chrysops X M. saxatilis*) | 56 days | 0,1,2,4% | 1% | Survival (98.3%)<br>Hematocrit (44.6%)<br>Lysozyme (939 U/ml)<br>NBT test (1.99 mg/ml)<br>Intracellular superoxide anion (0.897 $OD_{620nm}$)<br>Extracellular superoxide anion (2.679 nmol $O^{-2}$)<br>NBT test (< 0.3 $OD_{650nm}$) | Survival (98.3%)<br>Hematocrit (49.4%)<br>Lysozyme (811 U/ml)<br>NBT test (2.59 mg/ml)<br>Intracellular superoxide anion (1.039 $OD_{620nm}$)<br>Extracellular superoxide anion (3.694 nmol $O^{-2}$)<br>NBT test (1.337 ± 0.12 $OD_{650nm}$) | (Li and Gatlin III, 2003) |
| Common carp (*Cyprinus carpio*) | 60 days | 1% | 1% | Lysozyme 15th day (918 ± 16 U/ml)<br>RPS for *A.hydrophila* challenge (0%)<br>WBC (81.3 ± 2.7 x $10^3$cells/mm3) | Lysozyme 15th day (1546 ± 139 U/ml)<br>RPS for A.hydrophila challenge (64%)<br>WBC (97.2 ± 0.8 x $10^3$cells/mm3) | (Gopalakannan and Arul, 2010) |
| Rohu (*Labeo rohita*) | 60 | 1,2,4% | 1% | Serum globulin (2.38 ± 0.02 g/dl) | Serum globulin (2.6 ± 0.01 g/dl) | (Andrews et al., 2011) |
| Rohu (*Labeo rohita*) | 120 | 0.1,0.2,0.3% | 0.30% | The survival rate, respiratory burst activity significantly increased than control<br>Survival (66.3%)<br>NBT test (0.523)<br>Lysozyme activity (469 U/ml)<br>RPS for *A.hydrophila* challenge (33.33%) | Survival (88.1%)<br>NBT test (1.698)<br>Lysozyme activity (473.09 U/ml)<br>RPS for *A.hydrophila* challenge (76.18%) | (Mohseni et al., 2012) |
| Giant freshwater prawn, (*Macrobrachium rosenbergii*) | 75 days | 0,05,1,2% | 1% | Phenoloxidase activity, respiratory burst activity, and total hemocyte count were increased with increasing levels of BSY addition.<br>The ten-day challenge with white muscle disease virus resulted in the highest survival (70%) in 1% BSY added treatment | | (Parmar et al., 2012) |

**Table 6**
Economic and environment impact of optimal replacement of FM using BSY in relation to both farm and planetary levels.

| Species | Optimal FM replacement by BSY (%) | Fishmeal reduction (g/kg of feed) | | BSY inclusion (g/kg of feed) | | Net reduction in Feed production cost[c] (USD/kg of feed) | FCR | | Production cost reduction[d] (USD/t of fish) | Global fish production (tonnes) | Revenue generated in global aquaculture[e] (USD) | Reduction in fishmeal usage globally (tonnes) | Carbon footprint reduction in relation to the planetary production of fish[f] (tonne$CO_2$e) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Quantity (g) | Cost[a] (USD) | Quantity (g) | Cost[b] (USD) | | Control diet | BSY incoporated diet | | | | | |
| Rainbow trout (*Oncorhynchus mykiss*) | 30 | 200 | 0.290 | 300 | 0.165 | 0.125 | 1.13 | 1.37 | 95.00 | 959,689.77 | 91,170,528 | 262,955 | −318,701 |
| European sea bass (*Dicentrarchus labrax*) | 30 | 179 | 0.260 | 329 | 0.181 | 0.079 | 1.48 | 1.28 | 94.32 | 276,422.21 | 26,072,143 | 63,334 | −76,761 |
| Gilthead sea bream (*Sparus aurata*) | 30 | 200 | 0.290 | 300 | 0.165 | 0.125 | 1.88 | 1.92 | 120.00 | 282,073.82 | 33,848,858 | 108,316 | −131,279 |
| Thai Panga (*Pangasianodon hypophthalmus* X *Pangasius bocourti*) | 45 | 135 | 0.196 | 135 | 0.074 | 0.122 | 2.6 | 2.4 | 145.80 | 18,227.31 | 2,657,542 | 5906 | −7158 |
| Asian sea bass (*Lates calcarifer*) | 47 | 317 | 0.460 | 468 | 0.257 | 0.202 | 1.2 | 1.4 | 161.80 | 117,445.96 | 19,002,756 | 52,123 | −63,172 |
| Red drum juveniles (*Sciaenops ocellatus*) | 50 | 142 | 0.206 | 343 | 0.189 | 0.017 | 1.11 | 1.19 | 15.87 | 84,341.58 | 1,338,501 | 14,252 | −17,273 |
| Tilapia (*Oreochromis niloticus*) | 60 | 120 | 0.174 | 180 | 0.099 | 0.075 | 1.58 | 1.45 | 84.75 | 4,514,615.00 | 382,613,621 | 785,543 | −952,078 |
| Pacu (*Piaractus mesopotamicus*) | 50 | 120 | 0.174 | 190 | 0.105 | 0.070 | 1.04 | 1.05 | 68.81 | 15,214.28 | 1,046,819 | 1917 | −2323 |
| Climbing perch (*Anabas testudineus*) | 75 | 150 | 0.218 | 200 | 0.110 | 0.108 | 2.03 | 1.69 | 144.05 | 59,914.12 | 8,630,629 | 15,188 | −18,408 |
| Goldfish (*Carassius auratus*) | 45 | 180 | 0.261 | 266 | 0.146 | 0.115 | 3.32 | 2.34 | 227.11 | 382.63 | 86,898 | 161 | −195 |
| Giant freshwater prawn (*Macrobrachium rosenbergii*) | 40 | 103 | 0.149 | 155 | 0.085 | 0.064 | 5.07 | 5.53 | 34.61 | 294,018.46 | 10,177,155 | 167,470 | −202,974 |
| | | | | | | | | | **Total** | **6,622,345 Tonnes** | **576,645,450 USD** | **1,477,165 Tonnes** | **−1,790,324 (tonne$CO_2$e)** |

[a] Fishmeal cost = 1.45 USD/kg (average of 1300–1600 USD/Tonne); [b]BSY = cost 0.55 USD/kg (average of 0.5–0.6 USD/kg); [c]Net reduction in feed cost (USD/kg) = FM elimination cost – BSY inclusion cost.
[d] Fish production cost reduction (USD/ton of fish) = {Increment or decrement of feed cost per ton of fish production (1) X global production of corresponding species in tonnes (2)} (1) {[(control diet FCR – BSY diet FCR) X Net cost reduction per kg of feed production] + Net cost reduction per kg of fish peroductin] X 1000 (to convert into tonnes)}: (2) (FAO, 2022).
[e] Total revenue generated in global aquauclture (USD) = production cost reduction of fish (USD/ton of fish) X Global production of respective fish species (tonnes).
[f] Carbon footprint reduction = reduction in fishmeal usage globally by BSY incorporation (tonnes) X (−1.212 ton $CO_2$e) (corbon footprint value for one tonne of fishmeal production.

footprint of fishmeal production is more or less analogous worldwide. The computed carbon footprint value of global fishmeal production is about 4.65 megatonnes of $CO_2e$, using which the value of carbon footprint per tonne of fishmeal replacement was computed as −1.212 t $CO_2e$ (negative value represents a reduction of carbon emission) that used as a unit value for further sustainability calculation for individual fish species aquaculture. After computing these base calculation factors, a detailed assessment was carried out to evaluate the net cost savings and reduction of carbon footprint value in the production of different fish species using an optimally replaced fishmeal diet (Table 6).

From Table 6, it is ascertained that the net reduction in feed production cost coupled with enhanced FCR to fishmeal replaced BSY-based diet considerably reduced the production cost of different fish species (ranged 15.87–227.11 USD/t of fish). Besides, around 577 million USD revenue can be generated every year by the optimal replacement of fishmeal with BSY only from the aquaculture of the above-described fish species. In addition, these dietary fishmeal replacements also cause a massive impact on carbon footprint by reducing 1.79 megatonnes of $CO_2e$ globally every year. Still, the above values are not the comprehensive elucidation of the BSY potential in fishmeal replacement. If the 69% (as in fishmeal) of global production of BSY (0.49 MMT) is utilized for aquafeed production, around 13.94% (0.369 MMT of FM) of fishmeal usage can be replaced using BSY globally in aquafeed production every year (Appendix A3).

Apart from these, the BSY inclusion in fish nutrition will have additional advantages like inbuilt health promotors (immunostimulation, feed attractants, etc.), which substantially reduce the need for external feed additives and lead to further cost savings in the aquaculture sector. The reduced cost from BSY inclusion can be diverted into further development of this sector, like infrastructure development and the adoption of good hygienic protocols in the aquaculture chain. Besides, the inclusion of BSY in aquafeeds also reduces the pressure on capture fisheries of forage fishes for fishmeal production, which will support the marine food chain and indirectly augments commercial marine fisheries. Fish in fish out ratio (FIFO) is the critical sustainability indicator of aquaculture computed by quantifying the requirement of wild fish as feed input to produce a unit mass of farmed fish. The FIFO ratio of global aquaculture in the present situation is about 0.82:1 (IFFO, 2017). The replacement-caused fishmeal usage reduction (0.369 MMT) can further reduce the FIFO ratio from 0.82:1 to 0.71:1, thus improving sustainability.

## 8. Conclusion and future perspectives

The facts described critically in the present review on the potentiality and applicability of BSY in aqua feed production demonstrate that BSY can serve as an excellent protein source and partial replacer of fishmeal with functional health promotion activities in fish nutrition and apart from all, it helps in improving the sustainability in aquafeed production. The essential amino acid content of BSY is comparable with the fish meal except for arginine, lysine and methionine (Amorim et al., 2019; Chae et al., 2001; Podpora et al., 2016). The inability to complete fishmeal replacement may be due to the differential digestibility of individual EAAs of BSY in the different fish species. In this regard, systematic studies are warranted to understand the digestible amino acid levels in BSY and its physiological response in different fish species. Deciphering these responses needs extensive studies and field trials before the evidential conclusion towards the particular fish species. However, the probable range of BSY inclusion (10–31.5% for carnivores and 19–31.6% for omnivores) and fishmeal replacement using BSY based on feeding habits (30–50% for carnivores and 35–80.8% for omnivores) described in this review has multiple utilities among researchers to plan FM replacement trials using BSY in a new species; and feed manufacturers to incorporate optimal levels of BSY in the fish feeds depending on their feeding habit. In the future, some processing manipulation strategies will help improve the nutritional quality of BSY, especially in the initial stages of its life cycle. Storage temperature and time duration of collected spent yeast slurry from fermenters are the most critical factors in preserving the nutrition value of the final BSY biomass. Any dilation in these factors leads to autolysis of yeast cells and consequent protein loss (Huige, 2006). Hence the brewery infrastructure should be customized accordingly for achieving optimal temperature during the storage of live spent yeast slurry. Also, policies must be drawn that subsidize the establishment of valorization facilities and ensure proper market channels for BSY utilization will positively reduce the storage time duration of spent yeast slurry and prevent undesirable nutrient losses. The European Union Life Brewery Project (LIFE16ENV/ES/000160) identified the aquafeed industry as a potential consumer of BSY and also proposed the eco-design for the valorization process of BSY as an aquafeed ingredient (Iñarra et al., 2022). Genetically engineered yeast strains for increasing protein deposition in cell mass (Lübeck and Lübeck, 2022) and raw material fortification for efficient biomass production (Galili and Amir, 2013) and adapting enzymatic hydrolysis technique to increase digestibility (San Martin et al., 2020) are the emerging techniques for optimization of the nutritional profile and enhancing bio-assimilation values of the BSY. Up to now, fishmeal is the most suitable protein source in fish nutrition that also poses a copious amount of feed attractants (Taurine, etc.) and some unidentified growth factors (Hardy, 2010). Hence it is factorially tricky to replace fishmeal entirely with any other single alternative protein source. However, it is possible when multiple protein sources are used in optimal combination with exogenous enzymes supplementation or synthetic AA incorporation based on the requirements for individual fish species. To conclude, the aquaculture sector nowadays is efficiently progressing towards its sustainable feed supply, and BSY can be a valuable addition to this progress in the future.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## CRediT authorship contribution statement

**M. Gokulakrishnan:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Rajesh Kumar:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Supervision, Validation, Writing – review & editing. **Shajahan Ferosekhan:** Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – review & editing. **G.M. Siddaiah:** Formal analysis, Investigation, Methodology, Writing – review & editing. **S. Nanda:** Investigation, Supervision, Validation, Writing – review & editing. **Bindu R. Pillai:** Investigation, Supervision, Validation, Writing – review & editing. **S.K. Swain:** Investigation, Supervision, Validation, Writing – review & editing.

## Declaration of Competing Interest

None.

## Data availability

Data will be made available on request.

## Acknowledgments

The authors are thankful to the Director, ICAR-Central Institute of Freshwater Aquaculture, Kausalyaganga, Bhubaneswar, India and the Dean, College of Fisheries, OUAT, Bhubaneswar for providing all the necessary facilities and support for this review.

## Appendix A. Appendices

### A.1. Comparison of the fatty acid profiles of brewer's spent yeast (BSY) with the fish meal (FM)

| Fatty acids (g.kg$^{-1}$) | | BSY[a] | FM[b] |
|---|---|---|---|
| Lauric acid | C12:0 | 0 | 0.09 |
| Myristic acid | C14:0 | 1.5 | 4.4 |
| Palmitic acid | C16:0 | 1 | 13 |
| Palmitoleic acid | C16:1 | 14.3 | 5.3 |
| Stearic acid | C18:0 | 5.5 | 2.6 |
| Oleic acid | C18:1 | 4.5 | 9 |
| Linoleic acid | C18:2 | 2.4 | 1.5 |
| Linolenic acid | C18:3 | 0.9 | 1.4 |
| Stearidonic acid | C18:4 | 0 | 1.1 |
| Arachidic acid | C20:0 | 0 | 0.2 |
| Eicosenoic acid | C20:1 | 0 | 4.8 |
| Arachidonic acid | C20:4 | 0 | 1.7 |
| Eicosapentaenoic acid | C20:5 | 0 | 6.6 |
| Behenic acid | C22:0 | 0 | 0.2 |
| Erucic acid | C22:1 | 0 | 5.6 |
| Docosapentaenoic acid | C22:5 | 0 | 1.9 |
| Docosahexaenoic acid | C22:6 | 0 | 4.8 |
| Lignoceric acid | C24:0 | 0 | 0 |
| Total fatty acids | | 3.20% | 7.30% |
| ω6 | | 2.4 | 3.2 |
| ω3 | | 0.9 | 15.8 |
| ω3/ω6 | | 0.38 | 4.94 |

Data from Feedtables (http://www.feedtables.com).
[a] (Feedtables, 2017b); [b](Feedtables, 2017a).

### A.2. Comparison of the available micronutrients of brewer's spent yeast (BSY) with the fish meal (FM)

| Micronutrients | BSY[a] | FM[b] |
|---|---|---|
| (Vitamins) | | |
| Vitamin A (1000 IU/kg) | 0 | 0 |
| Vitamin D (1000 IU/kg) | 0 | 2.2 |
| Vitamin E (mg/kg) | 2.1 | 5.6 |
| Vitamin K (mg/kg) | 0 | 0 |
| Thiamine (mg/kg) | 91.5 | 0.2 |
| Riboflavin (mg/kg) | 42.5 | 7.9 |
| Niacin (mg/kg) | 480 | 127 |
| Pantothenic acid (mg/kg) | 119 | 13 |
| Pyridoxine (mg/kg) | 36.1 | 4.6 |
| Biotin (mg/kg) | 1.2 | 0.2 |
| Folic acid (mg/kg) | 11.2 | 0.3 |
| Cobalamines (mcg/kg) | 7.98 | 338 |
| Vitamin C (mg/kg) | 3.1 | 0 |
| Choline (mg/kg) | 3574 | 4138 |
| (Minerals) | | |
| Calcium (g/kg) | 3 | 44.8 |
| Phosphorus (g/kg) | 13.5 | 28.6 |
| Magnesium (g/kg) | 2.4 | 2.4 |
| Potassium (g/kg) | 22 | 8.5 |
| Sodium (g/kg) | 1.74 | 11.47 |
| Chlorine (g/kg) | 3.7 | 17.8 |
| Sulfur (g/kg) | 4.6 | 7.8 |
| Manganese (mg/kg) | 34 | 19 |
| Zinc (mg/kg) | 103 | 107 |
| Copper (mg/kg) | 20 | 12 |
| Iron (mg/kg) | 94 | 382 |
| Selenium (mg/kg) | 0.06 | 0.4 |
| Cobalt (mg/kg) | 0.6 | 0.1 |
| Molybdenum (mg/kg) | 1 | 0.2 |
| Iodine (mg/kg) | 1 | 2 |
| Electrolyte balance (mEq/kg) | 535 | 217 |
| Dietary cation-anion difference (mEq/kg) | 250 | 268 |

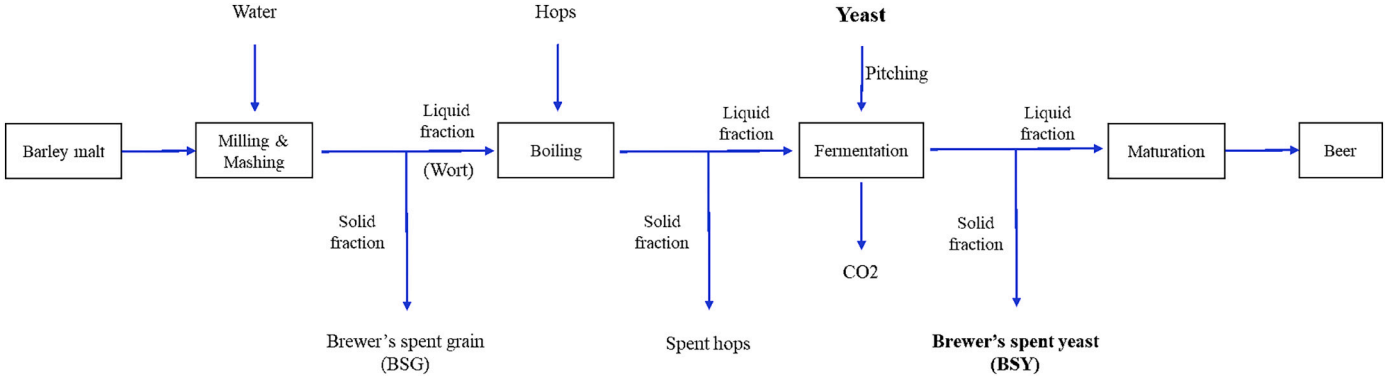
[a] (Feedtables, 2017b); [b](Feedtables, 2017a).

Data from Feedtables (http://www.feedtables.com).

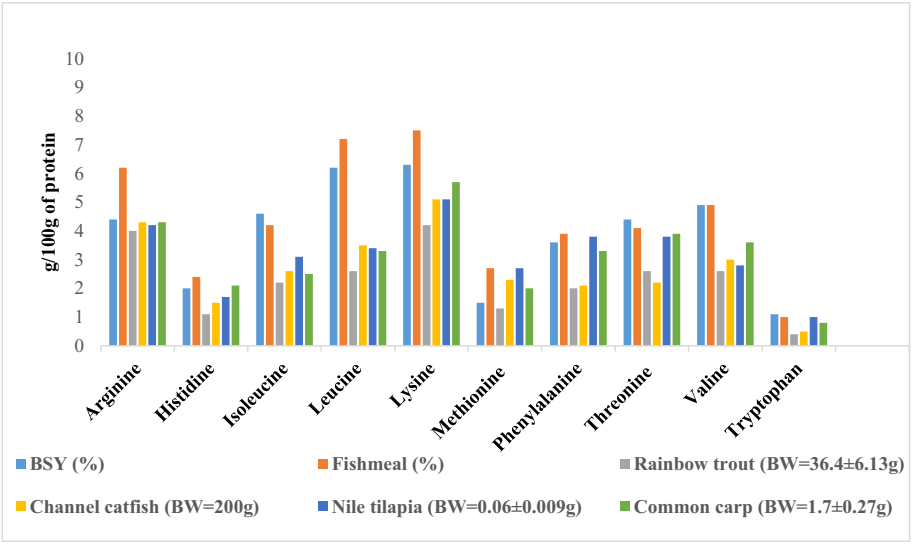
### A.3. Global potential of BSY in replacing fishmeal in aqua diets

| BSY | MMT | | Fishmeal |
|---|---|---|---|
| Total BSY production | 0.71 | 3.84 | Total fishmeal production |
| Assuming 69% of BSY to be used for aquaculture (as in fishmeal) | 0.4899 | 2.6496 | Fishmeal used for aquafeed production (69%) |
| Total available BSY protein (49% CP) | 0.24005 | 1.72224 | Total available fishmeal protein (65% CP) |
| Total possible fishmeal protein/biomass can be replaced by BSY (%) | 13.94% | | |
| Total possible fishmeal protein can be replaced by BSY (MMT) | 0.240 | | |
| Total possible fishmeal biomass can be replaced by BSY (MMT) | 0.369 | | |

*A.4. Flow digram of beer brewing and obtaining of brewer's spent yeast (BSY) (Marson t al., 2020; Mussatto, 2009)*




*A.5. Comparison of crude amino acid levels of BSY and fishmeal with AA requirements of some model fish species*




(Heuzé et al., 2018; Heuzé et al., 2015; NRC, 2011)

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